Schiffer.

The disclosure is objected to because the Applicants have embedded a hyperlink therein. Applicants submit that the instant amendment to page 10, whereby the links have been removed, rectifies this error. Withdrawal of the objection is respectfully requested.

Claims 10-14 are rejected per 35 U.S.C. 101 as being directed to nonstatutory subject matter. Per the Examiner's suggestion, independent claim 10 has been amended to recite purified moieties. Withdrawal of the §101 rejection is hereby solicited.

Claims 10-14 are rejected under 35 U.S.C. 112, second paragraph for containing "plurality of antigens", "capable of" and indefinite recitations regarding whether binding regions are bound to the recited moieties. Claim 10 is hereby amended to recite a dual binding feature. Claim 10 also is amended to clearly indicate that the non-binding and binding regions are contained on the same molecule. Claim 10 is further amended to recite that the moieties are derived from the same gene, and that the first binding region and the second binding region are situated at the first end and second end, respectively, of the molecule. In light of the foregoing amendment, withdrawal of the §112, second paragraph rejection is respectfully solicited.

Claims 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoogenboom et al (WO 93/06213). Claims 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevens et al.

Claim 14 is rejected under 35 U.S.C. 102(a) as being unpatentable over Stevens et al. or Hoogenboom et al in view of Goding and Skoog et al.

Independent claim 10 has been amended to recite the moieties being derived from the same gene. Support for this recitation can be found in originally filed claim 12, and also on page 3, lines 22-25 and page 7, lines 13-14 of the specification. Claim 10 also is amended to recite that the moieties comprising the molecule are engineered so that they are combined with each other in an unnatural configuration. Support for this recitation is found throughout the specification, and explicitly on page 5 line 27 through page 6, line 3.

Claim 15 has been added to further define each of the antigen binding sites in the

invented molecule. Specifically, each of the antigen binding sites are comprised of a CDR and an FR of a variable light chain protein. Support for this recitation is found in FIG. 2, and on page 7, lines 2-13 of the specification.

Applicants submit that in light of the amendments hereto, and the following remarks, the application is deemed in order for allowance.

Applicants' Invention

The instant invention comprises a bivalent molecule capable of binding two moieties. The molecule is useful in connecting similar or dissimilar ligands. The molecule is comprised of two identical subunits. A salient feature of the molecule is that its binding sites are each comprised of a complementary determining region juxtaposed to a framework region. This is contrary to "natural" aggregations wherein CDRs are juxtaposed side-by-side.

Hoogenboom et al Teaches Away

Claims 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoogenboom et al (WO 93/06213). Applicant respectfully disagrees. First, Hoogenboom suggests one binding site; the instant molecule, two.

Second, Hoogenboom suggests chimeric antibodies in an effort to "humanize" same to stymie rejection by the host. As such Hoogenboom requires portions of its engineered antibodies to be derived from different (human and non-human) sources. (See abstract) This feature teaches away from the "same gene" source recitation of now-amended independent claim 10.

It is noteworthy that Hoogenboom relies on a natural aggregation tendency of Fab fragments to produce a molecule (See page 6, lines 1-13 of Hoogenboom) . This contrasts with the recited molecule whereby subunits are engineered to cause identical units to be situated in a flipped or unnatural configuration.

It should also be noted that Hoogenboom's reliance on natural aggregation of antibody fragments "locks" that teaching's paradigm into a single antigen-binding site. As

can be noted on page 12, lines 10-25 of Hoogenboom, one iteration of the single binding site is comprised of a VL domain plus a VH domain.

Lastly, inasmuch as Hoogenboom deals with natural aggregates, Hoogenboom's eventual constructs are typical, with CDRs juxtaposed next to each other to form a binding site. This typical arrangement is illustrated in FIG. 1. Hoogenboom's arrangement contrasts vastly with the instant molecule wherein it is recited (in newly added claim 15) that each of its two binding regions are comprised of a CDR and a framework region.

In light of the foregoing amendment and argument, Applicants submit that Hoogenboom is not applicable art. Withdrawal of the §102 rejection based thereon is respectfully requested.

Stevens et al. Neither
Anticipates Nor Suggests
Counterpoising

Claims 10-13 are rejected under 35 U.S.C. §102(b) as being anticipated by Stevens et al. Applicants disagree. No where in Stevens is an unnatural aggregation of identical genetic expressions anticipated or suggested. No where in Stevens are two antigen binding sites anticipated or suggested.

Rather, Stevens is concerned with studying and modifying the natural combination two variable light chains to facilitate study of amyloid-deposition and diseases associated therewith. Also, the dimers disclosed in Stevens are variable light chains from different sources, and therefore are the result of the expression of different genes.

No mention is made in Stevens of engineered moieties juxtaposed in an unnatural configuration, as is now claimed in Independent Claim 10. No mention is made in Stevens of a molecule, comprised of two identical dimer subunits, which form two antigen binding sites.

Also, no mention is made in Stevens of an antigen binding site comprised of a CDR and an FR from a light chain protein, as is now recited in claim 15.

In light of the foregoing amendment and argument, Applicants submit that Stevens is not an applicable §102(b) reference. Withdrawal of same is respectfully solicited.

Hoogenbloom and Stevens
Do Not Suggest the Invention

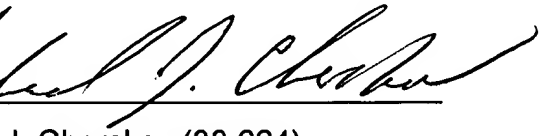
Claim 14 is rejected under 35 U.S.C. §103(a) as being unpatentable over Stevens et al. or Hoogenboom et al in view of Goding and Skoog et al. Applicants respectfully submit that in light of the foregoing traversal of Stevens and Hoogenboom, this §103 rejection is obviated.

Neither Stevens nor Hoogenboom, separately or combined, deals with multiple antigen binding sites. Also, neither Stevens nor Hoogenboom deals with engineering moieties aggregating in an unnatural configuration. Withdrawal of the 35 U.S.C. §103(a) rejection is respectfully requested. Lastly, the art of record does not suggest combining a CDR and a FR portion of identical molecules to produce an antigen binding site.

An earnest attempt has been made hereby to respond to the §101, §102, §103 and §112 rejections contained in the August 30, 2000 official action. Applicants submit that the instant amendment places the application in condition for allowance. If the Examiner feels that a telephonic interview will expedite allowance of the Application, she is respectfully urged to contact the undersigned. Reconsideration and allowance of claims 10-14, and consideration and allowance of newly added claim 15 is hereby solicited.

Respectfully submitted,

CHERSKOV & FLAYNIK

By 

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